Gene	11			12			22			F-ratio	p	Gene score
	N	Mean	SD	N	Mean	SD	N	Mean	SD			
Dopamine genes												
DRD1 SNP *Dde*I												
Lit												201
Optimized	39	20.10	10.2	164	17.58	11.1	133	18.30	10.9	0.848	0.43	201
DRD2 SNP *Taq* IA												
Lit												020
Optimized	15	15.93	10.3	120	19.50	10.2	201	17.51	11.4	1.560	0.21	021
DRD3 SNP *Msc*I												
Lit												202
Optimized	152	17.68	11.2	157	18.34	11.0	27	19.16	9.6	0.495	0.63	002
DRD4 [1] 48 bp repeat												
Lit												002
Optimized	56	19.00	10.9	162	17.98	10.5	118	17.86	11.6	0.223	0.80	200
DRD5 [2] dinucleotide repeat												
Lit												220
Optimized	74	18.63	11.4	111	19.15	11.3	151	17.38	10.6	0.881	0.41	120
DAT1 [3] repeat												
Lit												012
Optimized	21	15.33	12.4	142	17.41	10.9	173	19.07	10.8	1.619	0.20	012
Serotonin genes												
HTT[4] *(SLC6A4)* promoter ins/del												
Lit												022
Optimized	85	16.20	10.9	159	19.11	10.9	91	18.28	11.3	1.953	0.14	021
HTR1A SNP C-1918G												
Ind												022
Optimized	82	19.00	10.61	177	17.31	11.4	77	19.89	10.1	1.683	0.19	102

FIG. 1A-1

Gene	11			12			22			F-ratio	p	Gene score
	N	Mean	SD	N	Mean	SD	N	Mean	SD			
HTR1B (HTR1DB) SNP G861C												
Lit												002
Optimized	202	18.49	10.9	107	17.30	11.1	27	19.00	11.5	0.496	0.61	102
HTR1DA SNP T1350C												
Ind												02-
Optimized	266	18.16	11.3	70	19.34	9.7	_5	–	–	0.641	0.43	02-
HTR2A SNP T102C *MspI*												
Lit												012
Optimized	58	17.88	11.2	172	18.59	11.0	106	17.61	11.0	0.279	0.76	020
TDO2 SNP G-> A Int *6BsII*												
Lit												02-
Optimized	315	17.98	11.0	17	20.65	10.4	_5	–	–	0.951	0.33	02-
TPH SNP A 779 C												
Lit												002
Optimized	60	19.00	10.4	180	17.73	10.8	96	19.28	11.5	0.705	0.495	202
Norepinephrine genes												
DBH SNP *Taq* I												
Lit												220
Optimized	67	18.81	10.1	168	18.78	11.1	101	16.69	11.3	1.285	0.28	220
ADRA2A SNP promoter region *MspI*												
Ind												012
Optimized	186	17.42	11.1	128	18.8	10.5	22	21.95	11.7	1.96	0.14	012
ADRA2B del/ins												
Ind												102
Optimized	155	18.14	11.5	158	18.46	10.6	23	19.73	9.6	0.215	0.81	002
ADRA2C^{6} dinucleotide repeat												
Ind												202
Optimized	131	18.77	10.5	113	15.79	11.0	92	20.17	11.2	4.45	0.012	102

FIG. 1A-2

Gene	11			12			22			F-ratio	p	Gene score
	N	Mean	SD	N	Mean	SD	N	Mean	SD			
NET (SLC6A2) SNP A1970G *MnlI*												
Ind												120
Optimized	155	17.82	11.2	144	19.04	10.6	38	16.6	11.3	0.914	0.402	120
PNMT SNP G-148A												
Ind												012
Optimized	110	16.89	11.1	156	19.59	10.9	66	17.58	10.9	2.05	0.129	021
COMT SNP val 158 met, G1947A, *NlaIII*												
Ind												210
Optimized	75	19.42	10.8	175	18.52	11.0	86	16.52	10.8	1.55	0.212	210

Lit, references for literature-based gene scoring; Ind, gene scoring based on our studies of an independent set of subjects; SNP, single nucleotide polymorphism.

[1] *DRD4*: 11=any<4; 12=4/4; 22=any>4.

[2] *DRD5*: 11= 148/148; 12=het; 22=non 148/non 148.

[3] *DAT1*: 11=non 10/non 10; 12= 10/non 10; 22=10/10.

[4] *HTT*: 11=SS; 12=SL; 22=LL.

[5] *HTR1DA, TDO2* since there were only 2 22s, they were combined with the 12s.

[6] *ADRA2C*:11= <183/<183; 12=het; 22=183/183

FIG. 1A-3

Gene	11			12			22			F-ratio	p	Gene Score
	%	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.			
<u>Other Neurotransmitter Genes</u>												
HTR6 SNP (Shinkai et al. 1998)												
ADHD	2.8	12.33	9.7	27.1	18.26	10.3	70.0	18.66	11.2	1.44	.23	012
ODD		3.0	2.3		3.91	3.1		3.64	3.2	.44	.64	021
CD		2.11	1.5		3.65	2.6		3.17	2.6	2.05	.13	022
GABRB3 dinucleotide repeat (Mutirangura et al. 1992)[a]												
ADHD	38.0	18.99	10.8	47.9	17.48	11.1	14.1	19.69	10.9	1.05	.35	102
ODD		3.57	3.1		3.55	3.2		4.47	3.1	1.67	.18	002
CD		3.01	2.2		2.97	2.4		2.91	2.4	.089	.91	200
GABBR1 dinucleotide repeat (unpublished)[b]												
ADHD	9.5	17.5	11.7	27.0	19.1	11.7	63.5	18.2	10.5	.28	.752	020
ODD		3.54	3.7		3.66	3.1		3.72	3.1	.047	.953	012
CD		3.45	2.6		2.72	2.2		3.02	2.4	1.24	.291	201
CNR1 (Cannabinoid 1 receptor) (Dawson 1995)[c]												
ADHD	10.6	19.35	10.9	44.7	18.25	11.0	44.7	18.13	10.9	.174	.83	200
ODD		4.67	3.1		3.54	3.1		3.56	3.2	1.89	.15	200
CD		3.09	2.2		2.90	2.3		3.03	2.4	.146	.86	202
CHRNA4 (Cholinergic, nicotinic, alpha 4) (Weiland, Steinlein 1996)[d]												
ADHD	8.0	22.19	9.2	36.2	18.90	10.8	55.8	17.19	11.2	2.35	.096	210
ODD		5.07	3.0		3.59	3.0		3.55	3.2	2.74	.065	200
CD		3.11	2.1		2.93	2.3		2.99	2.4	.071	.930	200

FIG. 1B-1

NMDAR1 (Rupp et al. 1997) *Hpa* II SNP

ADHD	44.2	17.31	10.7	45.7	19.31	11.0	10.1	18.56	11.3	1.19	.303	021
ODD		3.79*	3.1		3.79*	3.1		4.84	3.1	2.93	.054	002
CD		2.83	2.3		3.07	2.3		3.28	2.7	.649	.523	012

ADORA2A (adenosine 2A receptor) (Deckert et al.1996) C 108 T *Rsa* I.

ADHD	33.2	19.95	10.4	44.7	17.57	11.0	22.0	18.97	10.8	1.48	.229	201
ODD		4.04	3.3		3.41	3.1		4.02	3.1	1.52	.219	202
CD		3.39	2.5		2.82	2.1		2.83	2.4	2.04	.131	200

GRIN2B (glutamate ionotropic, NMDA 2B receptor) T/G (SNP database WIAF-1189).

ADHD	20.9	17.94	10.6	52.3	19.35	10.6	26.8	18.10	11.1	.582	.559	021
ODD		3.03*	3.0		4.15	3.1		3.50	3.1	3.22	.041	021
CD		2.36*	2.0		3.28	2.4		2.98	2.3	3.59	.029	021

NOS3 (nitric oxide synthase 3) (Wang et al. 1996)

ADHD	67.5	18.50	10.9	25.0	18.60	10.6	7.5	17.12	11.6	.186	.830	220
ODD		3.72	3.1		3.87	3.3		3.29	3.1	.311	.733	120
CD		3.00	2.3		3.12	2.2		2.33	1.9	1.08	.339	120

Opoids

PENK (proenkephalin) (Weber, May 1990; Comings et al. 1999a)^{e}

ADHD	32.1	18.71	10.4	47.4	18.02	11.3	20.6	18.25	11.0	.053	.948	201
ODD		3.75	3.2		3.75	3.2		3.48	3.1	.255	.775	220
CD		3.03	2.4		3.00	2.4		2.92	2.2	.041	.959	220

FIG. 1B-2

MME (enkephalinase) (see Methods)^{f}.

ADHD	33.9	19.44	11.0	50.9	17.34	10.9	15.2	19.53	10.9	1.26	.284	202
ODD		3.98	3.25		3.44	3.1		3.95	3.0	1.00	.369	202
CD		3.10	2.4		2.81	2.3		3.32	2.4	1.08	.340	202

ANPEP (aminopeptidase N) (Watt, Willard 1990) and see Methods, A 257 G

ADHD	27.7	19.25	10.7	51.6	18.37	10.9	20.8	17.60	11.4	.398	.672	210
ODD		3.65	3.1		3.95	3.1		3.30	3.2	.945	.389	120
CD		3.12	2.4		3.05	2.4		2.42	2.0	1.96	.142	210

NAT1 (N-acetyl transferase) T 1088 A (Dietz et al. 1997; Comings et al. 2000)

ADHD	5.7	21.50	9.5	34.7	19.00	11.2	59.6	17.86	10.8	1.11	.329	210
ODD		4.94	3.7		3.51	3.2		3.68	3.1	1.58	.207	200
CD		4.11	2.8		3.00	2.3		2.88	2.2	2.26	.106	210

Hormones and neuropeptides

ESR1 (estrogen 1 receptor) dinucleotide repeat (del Senno et al. 1992; Comings et al. 1999).

ADHD	27.3	19.08	12.0	41.2	17.52	10.6	31.5	18.90	10.3	.673	.511	201
ODD		3.82	3.4		3.56	3.0		3.86	3.0	.293	.746	202
CD		3.26	2.6		2.53*	2.0		3.33	2.5	4.09	.017	202

CYP19 (aromatase cytochrome P - 450) dinucleotide repeat (Polymeropoulos et al. 1991b)^{g}

ADHD	13.4	16.88	11.6	45.2	17.28	11.7	41.4	19.76	9.9	2.11	.122	012
ODD		3.50	3.1		3.33	3.0		4.11	3.3	2.16	.116	102
CD		3.07	2.4		2.52*	2.2		3.37	2.4	4.61	.011	102

FIG. 1B-3

SHBP (sex hormone binding protein)(Xu,Li 1998)

ADHD	59.8	18.39	11.2	35.2	18.38	10.4	5.0	17.44	11.4	.057	.944	220
ODD		3.61	3.1		3.76	3.1		3.50	3.1	.108	.897	120
CD		2.85	2.3		3.11	2.3		3.06	1.8	.465	.628	021

CRH (corticosterioid releasing hormone) (*Xmn* I, Genome Database)

ADHD	89.8	18.25	11.1	8.6	18.78	8.8	1.5	25.00	7.9	1.189	.285	012
ODD		3.66	3.2		3.71	2.8		5.60	3.2	.972	.380	012
CD		2.96	2.4		3.10	2.1		3.80	3.3	.370	.691	012

OXTR (oxytocin receptor) (Liao et al. 1996) silent C->T in exon 3

ADHD	47.1	18.48	10.5	44.3	1 8.0	11.5	8.7	20.11	10.7	.431	.650	102
ODD		3.59	3.1		3.65	3.2		4.39	2.8	.776	.461	012
CD		2.77	2.3		3.14	2.3		3.14	2.4	1.06	.347	022

CCK C-45 T(Ishiguro et al. 1999)

ADHD	77.0	18.57	10.8	20.4	17.66	11.0	2.2	19.71	14.3	.227	.797	102
ODD		3.83	3.2		3.30	2.9		3.00	3.0	.909	.404	210
CD		3.04	2.4		2.71	2.2		3.14	2.3	.555	.574	102

INS (Hoban,Kelsey 1991; Gade-Andavolu et al. 1999)

ADHD	58.6	18.04	10.8	36.7	18.47	11.1	4.7	19.46	11.2	.147	.863	012
ODD		3.68	3.2		3.70	3.1		3.66	3.6	.0014	.998	120
CD		2.95	2.3		2.98	2.4		3.47	1.6	.334	.716	002

CD8 (Polymeropoulos et al. 1991a)[h]

ADHD	23.2	17.5	11.3	44.3	18.54	10.9	32.5	18.42	10.9	.122	.885	021
ODD		3.31	3.2		4.09	3.2		3.44	3.0	1.95	.143	021
CD		2.53	2.1		3.27	2.5		2.92	2.1	2.44	.088	021

FIG. 1B-4

INFG (Wu,Comings 1998)

ADHD	21.8	18.22	10.9	58.3	18.17	10.9	27.9	18.82	10.8	.109	.896	102
ODD		3.78	2.97		3.69	3.2		3.60	3.2	.068	.934	210
CD		3.11	2.4		3.01	2.4		2.82	2.0	.333	.717	210

PSI (Scott et al. 1996)

ADHD	36.0	17.78	11.1	48.0	18.56	10.6	15.2	18.19	11.6	.215	.806	021
ODD		3.44	3.3		3.92	3.1		3.57	3.1	.828	.438	021
CD		2.59	2.1		3.18	2.4		3.30	2.5	2.68	.069	012

*Significantly lower than highest value by tukey test at α = .05.

a 11 = <188/<188, 12 = het. 22 = =188/=188

b 11 = =10/=10, 12 = het. 22=>10/>10

c 11 = <5/<5 12=het. 22 = =5/=5

d 11 = =131/=131 12 = het. 22 = >131/>131

e 11 = =178/=178 12 = het. 22 = >178/>178

f 11 = a-c/a-c 12 = het. 22 = d-g/d-g

g 11 = <4/<4 12 = het. 22 = =4/=4

h 11 = 145/145 12 = 145/x 22 = x/x

FIG. 1B-5

Trait	r	r^2	adjusted r^2	F	p	# genes
ADHD	.466	.217	.16	3.82	<.0001	22
ODD	.443	.196	.14	3.58	<.0001	20
CD	.451	.203	.15	3.94	<.0001	19

FIG. 2

09/825,922
10/11

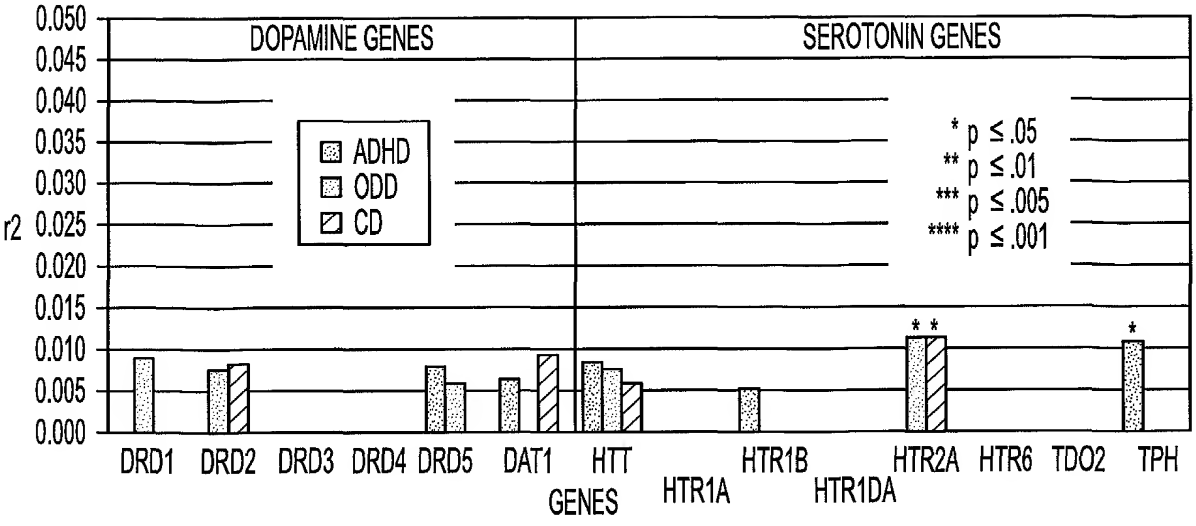


FIG. 3A

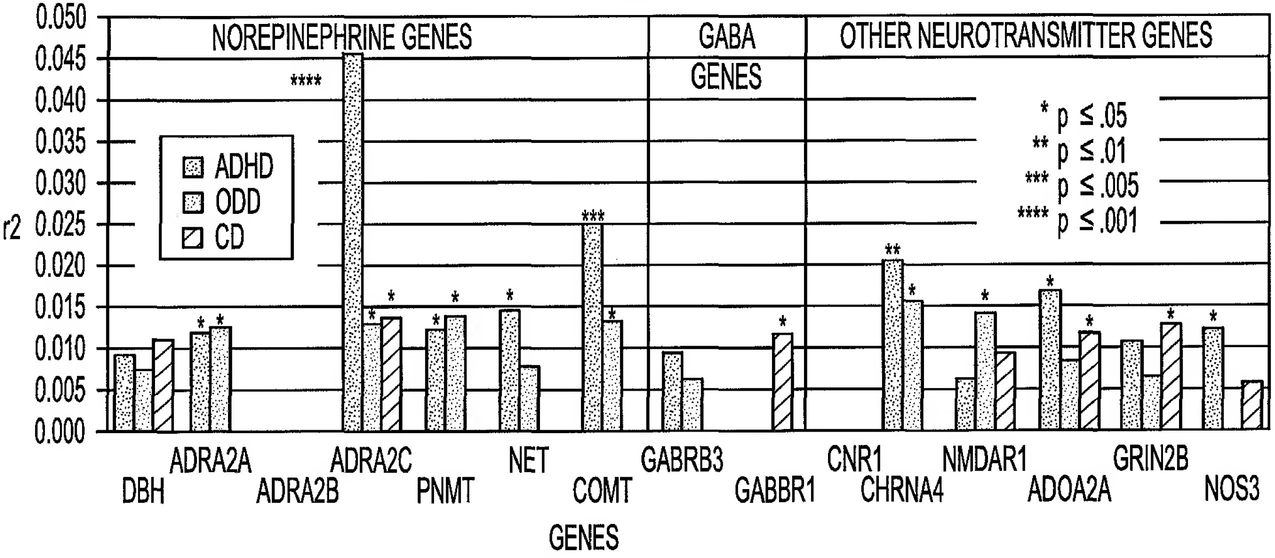


FIG. 3B

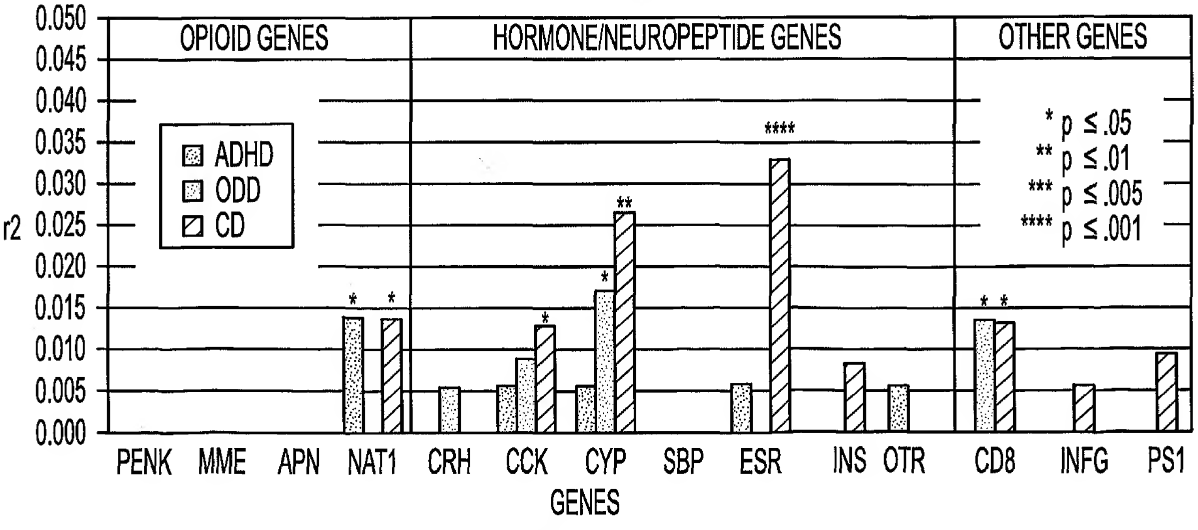
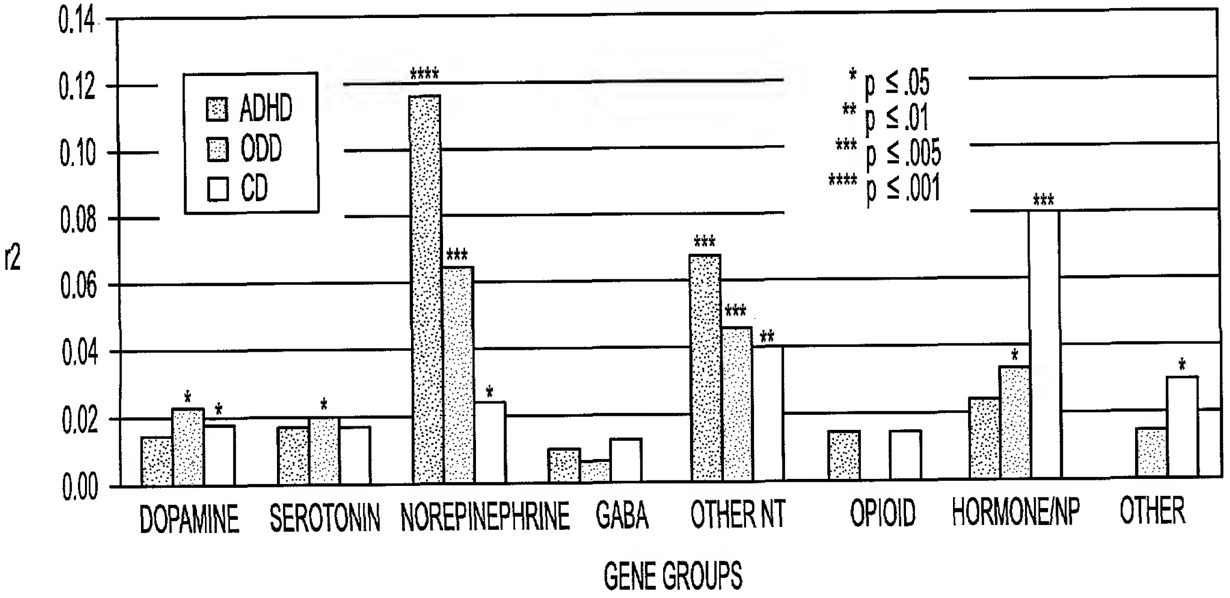


FIG. 3C


0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
r2
▨ ADHD
▨ ODD
☐ CD
* p ≤ .05
** p ≤ .01
*** p ≤ .005
**** p ≤ .001
*
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*
***
*
DOPAMINE
SEROTONIN
NOREPINEPHRINE
GABA
OTHER NT
OPIOID
HORMONE/NP
OTHER
GENE GROUPS

FIG. 4